The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: FFR103184
Title: A Randomised, Double-Blind, Placebo-Controlled, Parallel Group, Multicentre Two Week Study to Evaluate the Efficacy and Safety of Once-Daily, Intranasal Administration of GW685698X Aqueous Nasal Spray 100mcg* in Adult and Adolescent Subjects with Seasonal Allergic Rhinitis in Europe
Rationale: GW685698X (hereafter referred to as fluticasone furoate), the investigational drug for this study, is a novel corticosteroid with potent glucocorticoid activity. Fluticasone furoate is being developed as an aqueous nasal spray for the treatment of seasonal (SAR) and perennial allergic rhinitis (PAR). This study was conducted to evaluate the efficacy and safety of fluticasone furoate aqueous nasal spray 110mcg once daily (QD) in the treatment of SAR. To this end, fluticasone furoate was examined for the treatment of both nasal and ocular symptoms of allergic rhinitis. In the present study, four nasal symptoms (rhinorrohea, nasal congestion, nasal itching and sneezing) and three ocular symptoms (itching/ burning eyes, tearing/watering eyes and eye redness) were assessed twice daily by all subjects.
Phase: III
Study Period: 14 May 2005 – 22 August 2005
Study Design: After completing a 5- to 21-day screening period, eligible subjects were randomised to one of two treatment groups for a period of two weeks: fluticasone furoate aqueous nasal spray 110mcg once daily or vehicle Placebo nasal spray once daily. Males and females ≥12 years of age who were confirmed to have SAR and met the symptom requirements were eligible for enrolment. All efficacy measures were based on subject self-assessments. Throughout the study, subjects were not allowed to take any anti-allergy or rhinitis medication and were required to rate their nasal and non-nasal symptoms of allergic rhinitis on diary cards. After at least five days in the screening period, subjects who met the minimum symptom criteria could return to the clinic (Visit 2) to be randomised to one of two treatment arms. Subjects who did not meet the entry criteria after 21 days were not eligible for re-screening. Study randomisation was stratified by country and was centrally randomised within each country.
Centres: 23 centres in six countries: three centres in Estonia, four centres in Latvia, four centres in Lithuania, six centres in The Netherlands, three centres in the Russian Federation and three centres in Sweden.
Indication: Seasonal Allergic Rhinitis (SAR)
Treatment: Subjects meeting specified symptom criteria were randomized to 2 weeks treatment with fluticasone furoate nasal spray 110mcg once daily (QD) or vehicle placebo nasal spray QD. *NOTE: GW685698X aqueous nasal spray 110mcg (actual); Drug content of Fluticasone Furoate Nasal Spray was approximated at 25mcg/spray in all Phase 3 clinical trial documentation pending confirmation from final batch and stability testing. Final testing and analyses determined one spray to contain 27.5mcg of fluticasone furoate, equating to 110mcg for the recommended adult dose of two sprays administered to each nostril.
Objectives: The primary objective was to compare the safety and efficacy of once daily fluticasone furoate aqueous nasal spray 110mcg with vehicle Placebo nasal spray
Primary Outcome/Efficacy Variable: Mean change from baseline over the entire treatment period in daily reflective total nasal symptom scores (rTNSS) The total nasal symptom score (TNSS) was the sum of four individual symptom scores for rhinnorrhea, nasal congestion, nasal itching, and sneezing, where each symptom was scored on a scale of 0 to 3. The rTNSS was a rating of the severity of symptoms over the previous 12 hours and was performed in the morning (AM rTNSS) and evening (PM rTNSS). The daily rTNSS was the average of the AM rTNSS and PM rTNSS assessments.
Secondary Outcome/Efficacy Variable(s): (1) Mean change from baseline over the entire treatment period in morning (AM) pre-dose, instantaneous total nasal symptom scores (iTNSS) (2) Mean change from baseline over the entire treatment period in daily reflective total ocular symptom scores (rTOSS). The total ocular symptom score (TOSS) was the sum of three individual symptom scores for itching/burning eyes, tearing/watering eyes, and eye redness, where each symptom was scored on a scale of 0 to 3. The rTOSS was a rating of the severity of symptoms over the previous 12 hours and was performed in the morning (AM rTOSS) and evening (PM rTOSS). The daily rTOSS was the average of the AM rTOSS and PM rTOSS assessments. (3) Overall evaluation of response to therapy (4) Mean change from baseline to endpoint in the global score of the rhinoconjunctivitis quality of life questionnaire (RQLQ)
Statistical Methods: A total of 288 subjects were required for this study with 144 subjects in each of the two treatment groups: fluticasone furoate 110mcg aqueous nasal spray and vehicle placebo nasal spray. Data from GSK study

FFR20001 suggested a reasonable assumption for the standard deviation of mean change from baseline over the entire treatment period in daily rTNSS would be 2.6. Using a two-sample t-test with a two-sided significance level of 0.05, the chosen sample size provided 90% power to detect a difference of 1.0 between active treatment and placebo.
The primary population was the Intent-to-Treat (ITT) Population. The ITT Population was defined as all subjects who were randomized and received at least one dose of study drug. Unless otherwise specified, analyses based on the ITT Population included all available data for these subjects. This population will be the basis for all summaries, analyses, listings, and figures of demographic, efficacy, safety, and health outcomes data.
The primary analysis method was the pairwise comparison of treatment groups (fluticasone furoate vs. Placebo) using the analysis of covariance (ANCOVA) with adjustments for baseline daily rTNSS, investigative site, age, and gender.
The secondary efficacy measures concerning nasal and non-nasal symptoms were analyzed similarly by pairwise comparisons of the two treatment groups (fluticasone furoate vs. Placebo) using ANCOVA with adjustments for baseline values, investigative site, age, and gender. Overall evaluation of response to therapy was analysed using logistic regression adjusting for age, gender, investigative site, and treatment.
Multiplicity adjustments were made for the results from the primary efficacy, key secondary efficacy, and health outcomes endpoints. The primary efficacy endpoint served as a gatekeeper for the interpretation of treatment comparisons for the key secondary efficacy and health outcomes endpoints. To control for multiplicity across the key efficacy and health outcomes endpoints, statistical testing was performed in a sequential order as follows: 1) mean change from baseline over the entire treatment period in AM pre-dose iTNSS, 2) overall evaluation of response to therapy, and 3) the endpoints of mean change from baseline over the entire treatment period in daily rTOSS and mean change from baseline to endpoint in the global score of the RQLQ were controlled using Hochberg's method.

Study Population:

	Placebo	Fluticasone furoate (FF) 110mcg
Number of Subjects		
Planned, N	144	144
Randomised, N	144	141
Completed, n (%)	128 (89)	138 (98)
Total Number Subjects Withdrawn, n (%)	16 (11)	3 (2)
Withdrawn due to Adverse Events n (%)	2 (1)	0
Withdrawn due to Lack of Efficacy n (%)	9 (6)	1 (<1)
Withdrawn for other reasons n (%)	5 (3)	2 (1)
Demographics	Placebo	FF 110mcg
N (ITT)	144	141
Females: Males	80:64	71:70
Mean Age, years (SD)	29.4 (10.93)	30.7 (11.70)
White, n (%) Black Other Substitute the name of the predominant race(s) studied for the word "Race"	136 (94) 7 (5) 1 (<1)	135 (96) 4 (3) 2 (1)

Primary Efficacy Results: Daily rTNSS

	Placebo	FF 110mcg
LS Mean Change (SE)	-3.18 (0.20)	-4.94 (0.20)
LS Mean Difference	-1.757	
95% Confidence Interval	-2.28, -1.23	
p-value	<0.001	

Secondary Outcome Variable(s):

	Placebo	FF 110mcg
AM Pre-dose iTNSS		
LS Mean Change (SE)	-2.60 (0.19)	-4.50 (0.20)
LS Mean Difference	-1.898	
95% CI	-2.42, -1.38	
Daily rTOSS		
LS Mean Change (SE)	-2.26 (0.15)	-3.00 (0.15)
LS Mean Difference	-0.741	

95% CI	-1.14, -0.34	
Overall response to therapy		
Significantly Improved	19 (13)	50 (35)
Moderately Improved	37 (26)	45 (32)
Mildly Improved	39 (27)	30 (21)
No Change	34 (24)	16 (11)
Mildly Worse	6 (4)	0
Moderately Worse	7 (5)	0
Significantly Worse	2 (1)	0
Health Outcomes (Rhinoconjunctivitis Quality of Life Questionnaire):		
Overall	Placebo	FF 110mcg
LS Mean Change (SE)	-1.53 (0.10)	-2.23 (0.11)
LS Mean Difference		-0.701
95% CI		(-0.99, -0.41)
Safety Results: All AEs occurring during study participation were collected from the Screening visit through to the follow-Up phone call, three to five days after the end of treatment.		
	Placebo	FF 110mcg
Adverse Events During the Treatment Period	n (%)	n (%)
Subjects with any AE(s), n(%)	23 (16)	24 (17)
Headache	9 (6)	12 (9)
Epistaxis	2 (1)	4 (3)
Dizziness	2 (1)	2 (1)
Ear pain	3 (2)	1 (<1)
Dyspnoea	2 (1)	1 (<1)
Cough	0	2 (1)
Pharyngolaryngeal pain	0	2 (1)
Season al allergy	2 (1)	0
Serious Adverse Events - On-Therapy No fatal or non-fatal SAEs were reported during the study.		
Conclusion: See publications below		
Publications: Fokkens WJ, Jogi R, Reinartz S, Sidorenko I, Sitkauskiene B, van Oene C, Faris MA, Ellsworth A, Caldwell MF. Once daily fluticasone furoate nasal spray is effective in seasonal allergic rhinitis caused by grass pollen. Allergy 2007; 62:1078-1084. Fokkens W, Jogi R, Sidorenko I, Sitkauskiene B, van Tongeren J, Faris M, Ellsworth A, Caldwell M. Fluticasone furoate nasal spray (FFNS) 110 mcg once-daily is effective in seasonal allergic rhinitis (SAR) caused by grass pollen. Allergy 2007;62(Suppl. 83): 134 (abstract). Sidorenko I, Sitkauskiene B, Jogi R, Fokkens W, van Tongeren J, Faris M, Ellsworth A, Caldwell M. Efficacy of a novel enhanced-affinity glucocorticoid on ocular symptoms, fluticasone furoate nasal spray (FFNS) 110 mcg once-daily, in grass pollen-sensitive patients. Allergy 2007;62(Suppl. 83):134 (abstract).		

Dated updated: 6-Mar-2008